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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/016,146   | 12/10/2001  | Jay Cunningham       | 3078/04             | 7806             |
| 26648  | 7590        | 10/01/2004           | EXAMINER            |                  |
| PHARMACIA CORPORATION<br>GLOBAL PATENT DEPARTMENT<br>POST OFFICE BOX 1027<br>ST. LOUIS, MO 63006 |             |                      | SPIVACK, PHYLLIS G  |                  |
|  |             |                      | ART UNIT            | PAPER NUMBER     |
|  |             |                      | 1614                |                  |

DATE MAILED: 10/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/016,146

Applicant(s)

CUNNINGHAM ET AL.

Examiner

Phyllis G. Spivack

Art Unit

1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3,5,7 and 9-14 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3,5,7 and 9-14 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: \_\_\_\_\_.

Applicants' Request for Continued Examination (RCE) filed June 30, 2004 is acknowledged and accepted. Claims 10-13 are canceled. New claim 14 is presented. Claims 1, 3, 5, 7, 9 and 14 are now pending.

An Information Disclosure Statement filed September 29, 2003 is further acknowledged. Parent Application S.N. 09/262725 was obtained. Only the following references were present in the file and reviewed: B1, B2, B4, C2, C3, C4 and C5.

The disclosure is objected to for the following informalities: In claims 1, 5 and 9 "methotrexate" is misspelled.

Appropriate correction is required.

Following an amendment to claim 9, in which the claim was rewritten as an independent claim, the objection of record in the last Office Action is withdrawn.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5, 7 and 9-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-100 of copending Application No. 10/865414. Although the conflicting claims are not

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identical, they are not patentably distinct from each other because of overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1, 3, 5, 7 and 9-13 were rejected in the last Office Action under 35 U.S.C. 112, first paragraph, because, it was asserted, the specification does not reasonably provide enablement for treating or preventing any neoplastic disease.

Following the most recent amendments to claims 1 and 5, the claims are directed to preventing or inhibiting any solid tumor growth comprising administering a compound of the formula of instant claims 1 and 5, together with one of fourteen recited chemotherapeutic agents, and pharmaceutical compositions thereto, claim 9. The instant specification fails to provide guidance that would allow the skilled artisan background sufficient to practice the instant invention without resorting to undue experimentation. The specification provides support for showing an additive effect following the administration of compound XII with cyclophosphamide or cisplatin to treat two distinct tumor cell lines.

In response, Applicants have replaced the phrase "treating or preventing neoplastic disease" with "preventing or inhibiting solid tumor growth".

Applicants' argument is not persuasive. The rejection is repeated for the reasons of record.

Each particular solid tumor has its own specific characteristics and etiology. The unpredictability observed with single agent therapy is compounded when a combination

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of agents is employed. The broad recitation "preventing or inhibiting solid tumor growth" is inclusive of many pathologies that presently have no established successful therapies.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 3, 5, 7 and 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruminski et al., WO 97/08145, and Remington's Pharmaceutical Sciences.

Ruminski teaches compounds that differ from those presently claimed in the formula of instant claims 1, 5 and 9 by the position of one halide. See the second and third compounds on page 791 and the first and second compounds on page 792. The compounds are taught to be useful to treat and inhibit solid tumor growth. See page 12, lines 28-33. It would have been reasonable to expect compounds of such close structural similarity, i.e., as position isomers, to demonstrate the same ability to antagonize integrin  $\alpha v \beta 3$  and exhibit anti-solid tumor growth properties. Motivation to combine other active ingredients, and to prepare a pharmaceutical composition comprising the claimed compounds with other known antineoplastic agents, is provided on page 29, lines 22-23. Remington discloses two established anti-neoplastic agents, cyclophosphamide and fluorouracil. In view of the two references, one skilled in the oncology art would have been motivated to prepare a pharmaceutical composition

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comprising the compounds disclosed by Ruminski with cyclophosphamide or fluorouracil. Such would have been obvious in the absence of evidence to the contrary because both are well established in the prior art as anti-neoplastic agents.

It is generally *prima facie* obvious to use in combination two or more ingredients that have previously been used separately for the same purpose. In re Kerkhoven, 205 USPQ 1069.

Specific statements in the references that would spell out the claimed invention are not necessary to show obviousness since questions of obviousness involve not only what references expressly teach, but also what they would collectively suggest to one of ordinary skill in the art. It would have been reasonable to expect an additive advantage of the combined agents in the treatment or inhibition of solid tumor growth.

No claim is allowed.

Nickols et al., Proceedings of the American Association for Cancer Research, is cited to show further the state of the art. Applicants are requested to show the structures of the referenced compound "S448".

Any inquiry concerning this communication should be directed to Phyllis G. Spivack at telephone number 571-272-0585.

*Phyllis Spivack*

Phyllis G. Spivack  
Primary Examiner  
Art Unit 1614

**PHYLLIS SPIVACK  
PRIMARY EXAMINER**

September 30, 2004